SUPPORT FOR THE AMENDMENTS

The present amendment cancels claims 4-11, 16 and 17, amends claims 1, 3 and 19, and adds new claims 21-30. Support for these amendments is provided by the originally filed claims and specification.

Support for the amendment to claim 1 can be found, for example, at paragraphs [0017], [0018], [0035], [0050]-[0057], [0066] and [0067], as well as original claims 8, 10 and 17, of Kubo (U.S. 2007/0224282), which is the U.S. pre-grant publication of the originally filed application.

Support for the amendment to claims 3 and 19, and newly added claims 21-30, can be found, for example, at paragraphs [0022]-[0027], as well as original claims 2 and 3, of Kubo.

It is believed that these amendments have not resulted in the introduction of new matter.

REMARKS

Claims 1-3, 12-15 and 18-30 are currently pending in the present application. Claims 4-11, 16 and 17 have been cancelled, claims 1, 3 and 19 have been amended, and new claims 21-30 have been added, by the present amendment.

The rejection of claims 1-8, 10-15 and 17-20 under 35 U.S.C. § 103(a) as being obvious over Bosch (U.S. Patent 5,510,118) in view of Yamakawa (Journal of Controlled Release) is obviated by amendment, with respect to claims 1-3, 12-15 and 18-30, which incorporates into amended claim 1 the limitation that the poorly soluble drug is 1-cyclopropyl-8-methyl-7-[5-methyl-6-(methylamino)-3-pyridinyl]-4-oxo-1,4-dihydro-3-quinolinecarboxylic acid (hereinafter referred to as "T-3912"), and the unexpected results set forth in the 37 C.F.R. § 1.132 Declaration appended herewith.

Amended claim 1 is now directed to a process for producing a fine dispersion of the poorly soluble drug T-3912, wherein the process comprises: suspending T-3912 in a liquid containing no deflocculant to obtain a suspension; introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion; and adding a deflocculant to the dispersion to deagglomerate aggregated particles contained therein.

Yamakawa describes T-3912.

Unlike the process of the present invention, Bosch describes that the surface modifier is preferably present before microfluidization (See e.g., column 7, lines 55-56). Bosch mentions that if the surface modifier was not added before microfluidization, then the surface modifier must be added thereafter (See e.g., column 8, lines 16-18). Based on the disclosure of Bosch, a skilled artisan would reasonably expect that fine dispersions of a poorly soluble drug would exhibit either slightly improved properties if the surface modifier is added before

microfluidization in accordance with the preferred embodiment described therein, or similar properties regardless of whether the surface modifier is added before or after microfluidization.

Contrary to the disclosure of Bosch however, as shown by the comparative experimental data presented in Table A of the 37 C.F.R. § 1.132 Declaration appended herewith, which is reproduced hereinbelow for the Examiner's convenience, Applicants have discovered that a fine dispersion of the poorly soluble drug T-3912 surprisingly exhibits superior properties with respect to a narrow particle size distribution and an improved dispersion stability when produced by the process of present invention, which comprises suspending T-3912 in a liquid containing no deflocculant to obtain a suspension, introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, and adding a deflocculant to the dispersion to deagglomerate aggregated particles contained therein, as presently claimed.

Table A

Examples	Poorly Soluble Drug	Deflocculant	Particle Size Distribution	
			50% Cumulative Diameter (nm)	90% Cumulative Diameter (nm)
Example A	T-3912	Added After Attrition	205	374
Comparative Example B	T-3912	Present in Premix	1443	4810
Comparative Example C	Naproxen	Added After Attrition	514	1061
Comparative Example D	Naproxen	Present in Premix	320	653

The inventive fine dispersion of Example A, which was produced by a process comprising suspending *T-3912* in a liquid containing *no deflocculant* to obtain a suspension, introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, and *subsequently adding a deflocculant* to the dispersion to deagglomerate aggregated particles contained therein, in accordance with an exemplary aspect of the present invention, surprisingly exhibited *superior* properties with respect to a narrow particle size distribution and an improved dispersion stability.

In contrast, the fine dispersion of Comparative Example B, which was produced by a process comprising suspending *T-3912* in a liquid *containing deflocculant* to obtain a suspension, and introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, exhibited *inferior* properties with respect to an undesirably wide particle size distribution and a reduced dispersion stability.

Meanwhile, the fine dispersion of Comparative Example C, which was produced by a process comprising suspending the poorly soluble drug *Naproxen*, as described and exemplified in Bosch, in a liquid containing *no deflocculant* to obtain a suspension, introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, and *subsequently adding a deflocculant* to the dispersion to deagglomerate aggregated particles contained therein, exhibited *inferior* properties with respect to an undesirably wide particle size distribution.

In contrast, the fine dispersion of Comparative Example D, which was produced by a process comprising suspending the poorly soluble drug *Naproxen*, as described and exemplified in Bosch, in a liquid *containing deflocculant* to obtain a suspension, and introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, exhibited *almost identical* properties to Comparative Example C with respect to a particle size distribution.

This evidence clearly demonstrates that a fine dispersion of T-3912, which surprisingly exhibits superior properties with respect to a narrow particle size distribution and an improved dispersion stability, is unexpectedly produced by the process of the present invention comprising suspending T-3912 in a liquid containing no deflocculant to obtain a suspension, introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, and adding a deflocculant to the dispersion to deagglomerate aggregated particles contained therein, as presently claimed.

This evidence also demonstrates that contrary to page 9, lines 15-22 of the Official Action, the process of Bosch does not intrinsically produce a fine dispersion of any poorly soluble drug that exhibits superior properties with respect to a narrow particle size distribution and an improved dispersion stability, as alleged by the Office.

Bosch and Yamakawa, when considered alone or in combination, fail to recognize that a fine dispersion of T-3912 which exhibits superior properties with respect to a narrow particle size distribution and an improved dispersion stability can be produced by a process comprising suspending T-3912 in a liquid containing no deflocculant to obtain a suspension, introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, and adding a deflocculant to the dispersion to deagglomerate aggregated particles contained therein, as presently claimed, thereby precluding a *prima facie* case of unpatentability.

Withdrawal of this ground of rejection is respectfully requested.

In conclusion, Applicants submit that the present application is now in condition for allowance and notification to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, L.L.P.

Richard L. Treanor
Attorney of Record
Registration No. 36,379

David P. Stitzel
Attorney of Record
Registration No. 44,360

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 07/09)